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L17 0 L15

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L1 STRUCTURE UPLOADED

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L3 0 S L1 FUL

L4 STRUCTURE UPLOADED

L5 27 S L4 FUL

FILE 'CAPLUS' ENTERED AT 22:55:33 ON 12 AUG 2001

L6 21 S L5

FILE 'REGISTRY' ENTERED AT 23:00:12 ON 12 AUG 2001

L7 STRUCTURE UPLOADED

L8 0 S L7 FUL

L9 STRUCTURE UPLOADED

L10 0 S L9 FUL

L11 STRUCTURE UPLOADED

L12 STRUCTURE UPLOADED

L13 0 S L12 FUL

FILE 'CAPLUS' ENTERED AT 23:09:00 ON 12 AUG 2001

FILE 'REGISTRY' ENTERED AT 23:17:13 ON 12 AUG 2001

L14 STRUCTURE UPLOADED

L15 0 S L14

L16 9 S L14 FUL

FILE 'CAPLUS' ENTERED AT 23:23:36 ON 12 AUG 2001

L17 0 S L15

=> s l16

L18 14 L16

=> d 1-5 bib abs

L18 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2001 ACS

AN 2001:152645 CAPLUS

DN 134:193224

TI Fluorenone compounds with modified 7-position substituents for treating and preventing brain and spinal injury

IN Cragoe, Edward J., Jr.; Marangos, Paul J.; Weimann, Torsten R.

PA Questcor Pharmaceuticals, Inc., USA

SO PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DT Patent

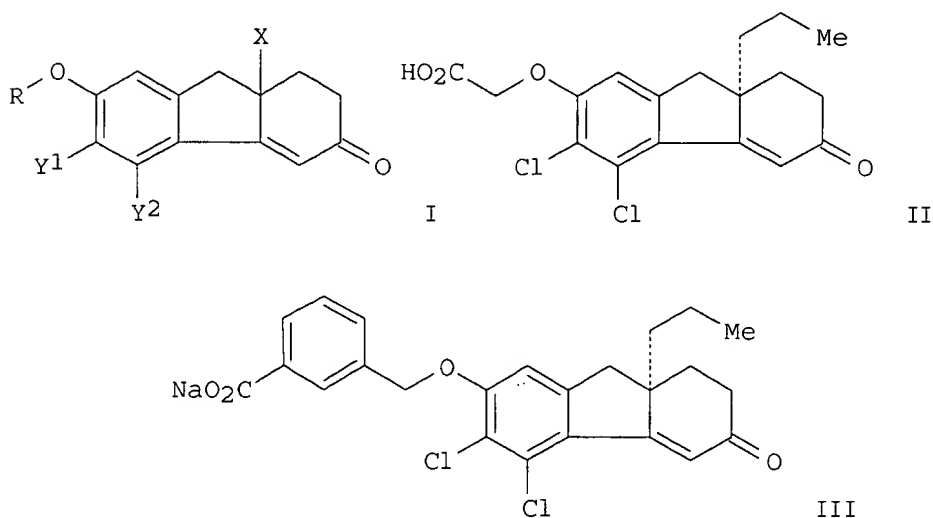
LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2001014334 A1 20010301 WO 2000-US22990 20000822
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 6251898 B1 20010626 US 1999-379656 19990824
PRAI US 1999-379656 A 19990824
US 1999-379816 A 19990824
OS MARPAT 134:193224
GI



AB New neuroprotective drugs are disclosed, which are analogs of certain previously known fluorenone compds. The new analogs have structure I [where X is a lower alkyl, substituted alkyl, or cycloalkyl group, R is selected from certain types of ether, ester, or amide groups, and Y1 and Y2 are halogen, H, or Me]. I potentially inhibit the unwanted release of excitotoxins by astrocyte cells following an injury or insult to the brain or spinal cord. The compds. are more than 30 times more potent than the previously known lead compd., L-644,711 (II), in reducing aspartate release by stressed astrocyte cells. I can also help reduce swelling in astrocyte cells, and can thereby help promote proper blood flow through the brain following a head injury or other crisis. Accordingly, I can reduce brain or spinal cord damage caused by a hypoxic, ischemic, infective, inflammatory, or other injury, crisis, or insult to the brain or spinal cord. As an illustration, several examples were prepd. and tested. For instance, cleavage of the carboxymethyl group from II (ref. given) gives a phenolic intermediate, which was re-etherified with Me 3-(bromomethyl)benzoate and then sapond. to give the sodium salt III. I were very efficacious in several in vitro animal models of focal or global brain ischemia. In a test for suppression of excitotoxin release by stressed astrocytes, III had a potency of 3,378% compared to the benchmark compd. II (100%). The structure-activity relationship resulting in the increased potency of the new compds. is described.

- (1) Cragoe; US 4356313 A 1982 CAPLUS
- (2) Cragoe; US 4731471 A 1998 CAPLUS
- (3) Pietruszkiewicz; US 4731470 A 1988 CAPLUS
- (4) Woltersdorf; US 4797391 A 1989 CAPLUS

L18 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2001 ACS

AN 1989:496878 CAPLUS

DN 111:96878

TI Preparation of [(5,6-dichloro-3-oxo-9,9a-disubstituted-2,3,9,9a-tetrahydrofluoren-7-yl)oxy]alkanoic acids and -alkanimidamides and their pharmaceutical compositions for treatment of gray matter edema

IN Woltersdorf, Otto W., Jr.; Cragoe, Edward J., Jr.; Pietruszkiewicz, Adolph M.

PA Merck and Co., Inc., USA

SO U.S., 15 pp. Cont. of U. S. Ser. No. 910,924, abandoned.

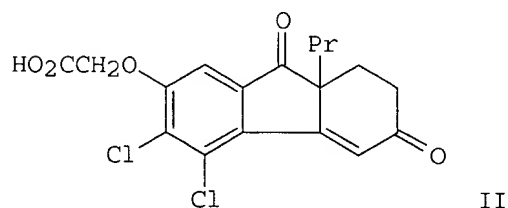
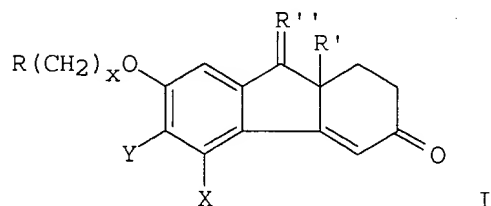
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4797391	A	19890110	US 1988-150462	19880208
PRAI	US 1986-910924		19860924		
OS	MARPAT 111:96878				
GI					



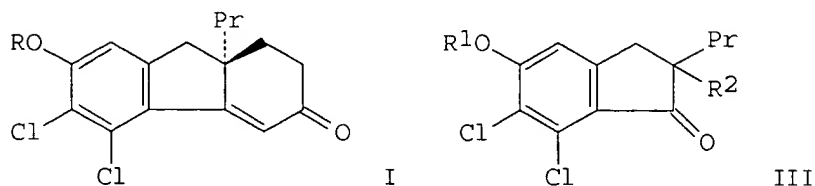
AB The title compds. [I; R = CO₂R₁, C(:R₃)R₂; R' = alkyl, (halo)aryl, aralkyl, cycloalkyl, cycloalkylalkyl; R'' = O, or H plus OH, Cl, Br, Me, NH₂, N₃, alkanoyloxy, or NHP(O)(OEt)₂; R₁ = H, alkyl, carboxyalkyl; R₂ = NH₂, NHR₄, NR₄R₅; R₃ = NH, NR₄; R₄, R₅ = alkyl, amino (R₄ and R₅ may not both be amino); R₂R₃, R₄R₅ may form rings; X, Y = halo, alkyl; x = 1-4] and related compds. were prepd. as agents for treating brain edema (no data). 5,6-Dichloro-1,2,9,9a-tetrahydro-7-methoxy-9a-propyl-3H-fluoren-3-one underwent successive benzylic bromination with NBS, hydrolysis of the 9-bromo deriv. by AgNO₂ in aq. MeOCH₂CH₂OH, Jones oxidn. of the 9-alc., demethylation of 7-MeO by pyrolysis with pyridine-HCl, alkylation of 7-OH by BrCH₂CO₂Et and K₂CO₃ in DMF, and sapon. by aq. NaOH/EtOH, to give (fluorenyloxy)acetic acid II. A parenteral soln. of II.Na was prepd. from 500 mg II, 5.6 mL 0.25 N NaHCO₃, and H₂O to make 10 mL.

L18 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2001 ACS

AN 1988:167131 CAPLUS

DN 108:167131
 TI Preparation of an enantiomer of a substituted fluorenyloxyacetic acid for treating brain edema
 IN Conn, Robin S. E.; Karady, Sandor
 PA Merck and Co., Inc., USA
 SO U.S., 6 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 1

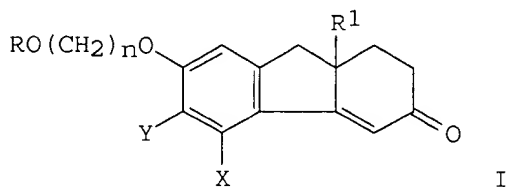
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4704472	A	19871103	US 1985-797311	19851218
GI					



AB The title acid (I; R = CH₂CO₂H) (II), useful in treating brain edema (no data), is prepd. Stirring a mixt. of indanone III (R₁ = Me, R₂ = H) with MeCOCH:CH₂, dihydro-3,4-dichlorobenzylcinchonidinium chloride, and KOH in MePh gave 92% III (R₁ = Me, R₂ = MeCOCH₂CH₂) as a 70 : 30 R- and S-isomer mixt. which was cyclized with H₂SO₄ at 65-75.degree. to give the phenolic I (R = H) (IV) after hydrolysis over SnCl₄ in situ. Substitution of IV with ClCH₂CO₂Et over K₂CO₃, NaI, and Triton X-405 gave 96.6% ester I (R = CH₂CO₂Et) which was sapond. to give 89.8% II as a 76:24 R- and S-isomer mixt.

L18 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2001 ACS
 AN 1987:515380 CAPLUS
 DN 107:115380
 TI Preparation of [(5,6-dichloro-3-oxo-9a-propyl-2,3,9,9a-tetrahydrofluoren-7-yl)oxy]ethanol and its derivatives as agents for treating brain injuries
 IN Cragoe, Edward J., Jr.
 PA Merck and Co., Inc., USA
 SO U.S., 9 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4675341	A	19870623	US 1986-896022	19860813
GI					



AB Title compds. I [X, Y = halo, alkyl; R = H, C(O)(CH₂)_mNMe₂,

C(O)CH₂CH₂CO₂H, C(O)CH:CH₂CO₂H; R₁ = alkyl, cycloalkyl, aralkyl, (halo)aryl; n = 1-4; m = 1-3] are prepd. as agents used for treating brain injury (no data). A mixt. contg. 3.36 mmol each of DBN and 4-(dimethylamino)butyric acid hydrochloride and also (R)-(+)-[(5,6-dichloro-1,2,9,9a-tetrahydro-9a-propyl-1H-fluoren-7-yl)oxy]ethanol (amt. not specified) was stirred for 16 h to give 1.03 g I [X = Y = Cl, R = Me₂N(CH₂)₃C(O), R₁ = Pr, n = 2] (II). Capsules were formulated contg. II 108.4, lactose 90.6, and Mg stearate 1 mg/capsule.

L18 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2001 ACS

AN 1987:156087 CAPLUS

DN 106:156087

TI [(2,3,9,9a-Tetrahydro-3-oxo-9a-substituted-1H-fluoren-7-yl)oxy]ethanimidamides and [(2,3,9,9a-tetrahydro-3-oxo-9a-substituted-1H-fluoren-7-yl)oxy]ethanimidic acid hydrazides, their derivatives and their salts

IN Cragoe, Edward J., Jr.; Woltersdorf, Otto W., Jr.

PA Merck and Co., Inc., USA

SO U.S., 9 pp.

CODEN: USXXAM

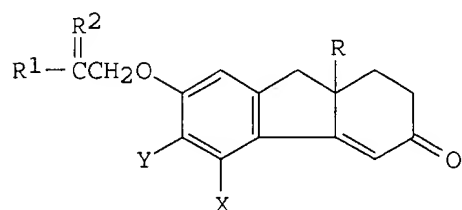
DT Patent

LA English

FAN.CNT 1

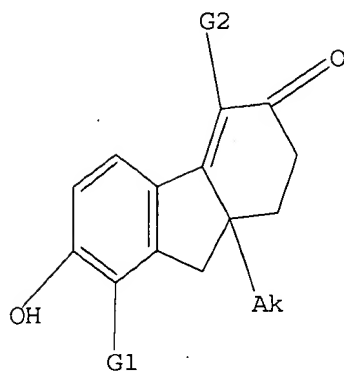
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PI	US 4604396	A	19860805	US 1985-780145	19850926
	CA 1284329	A1	19910521	CA 1986-518544	19860918
	DK 8604572	A	19870327	DK 1986-4572	19860925
	EP 217287	A2	19870408	EP 1986-113183	19860925
	EP 217287	A3	19880720		
	EP 217287	B1	19910626		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	ES 2001801	A6	19880616	ES 1986-2184	19860925
	AT 64733	E	19910715	AT 1986-113183	19860925
	JP 62084052	A2	19870417	JP 1986-226326	19860926
PRAI	US 1985-780145		19850926		
	EP 1986-113183		19860925		

GI



AB Title compds. I (R = alkyl, aryl, haloaryl, aralkyl, cycloalkyl, cycloalkylalkyl; R₁ = NH₂, NHR₃, NR₃R₄; R₂ = NH, NR₃; R₃, R₄ = alkyl, amino; wherein R₁ and R₂ may be joined together via R₃ to form a heterocyclic ring of 5 or 6 atoms contg. 2N; NR₃R₄ = heterocycle; X, Y = halo, alkyl); and their pharmaceutically acceptable salts, useful in the treatment of gray matter edema, are prepd. I are devoid of the pharmacodynamic, toxic, or various side effects characteristic of the diuretics, steroids, and barbiturates used in current therapy. Thus, [R-(+)]-5,6-dichloro-9a-propyl-7-hydroxy-2,3,9,9a-tetrahydro-1H-fluoren-3-one was treated with K₂CO₃ and ClCH₂CN to give the fluorenyloxyacetonitrile deriv., which was treated first with NaOMe and then with NH₄Cl to give [R-(+)]-I.HCl (R = Pr, R₁ = NH₂, R₂ = NH, X = Y =

=> d
L14 HAS NO ANSWERS
L14 STR



G1 H, CF2, OH, Cl, F

G2 H, Me, Et, n-Pr, CF3, CN, C(O)CH3, Cl

Structure attributes must be viewed using STN Express query preparation.

=> s l14
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SAMPLE SCREEN SEARCH COMPLETED - 24100 TO ITERATE

4.1% PROCESSED 1000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 472755 TO 491245
PROJECTED ANSWERS: 0 TO 0

L15 0 SEA SSS SAM L14

=> s l14 ful
FULL SEARCH INITIATED 23:22:49 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 488090 TO ITERATE

82.0% PROCESSED 400000 ITERATIONS 9 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.16

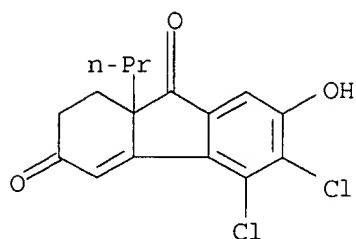
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PROJECTED ANSWERS: 9 TO 19

L16 9 SEA SSS FUL L14

=> d 1-9

L16 ANSWER 1 OF 9 REGISTRY COPYRIGHT 2001 ACS
RN 121913-84-6 REGISTRY
CN 1H-Fluorene-3,9(2H,9aH)-dione, 5,6-dichloro-7-hydroxy-9a-propyl- (9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C16 H14 Cl2 O3
SR CA

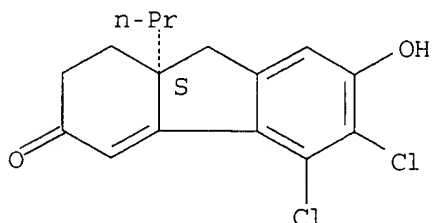
LC STN Files: CA, CAPLUS, USPATFULL



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L16 ANSWER 2 OF 9 REGISTRY COPYRIGHT 2001 ACS
RN 105615-51-8 REGISTRY
CN 3H-Fluoren-3-one, 5,6-dichloro-1,2,9,9a-tetrahydro-7-hydroxy-9a-propyl-,
(S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C16 H16 Cl2 O2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, USPATFULL
(*File contains numerically searchable property data)

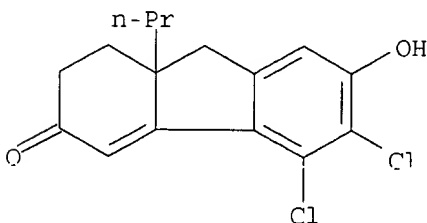
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L16 ANSWER 3 OF 9 REGISTRY COPYRIGHT 2001 ACS
RN 101833-21-0 REGISTRY
CN 3H-Fluoren-3-one, 5,6-dichloro-1,2,9,9a-tetrahydro-7-hydroxy-9a-propyl-,
(+)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C16 H16 Cl2 O2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
(*File contains numerically searchable property data)

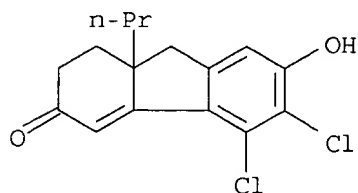
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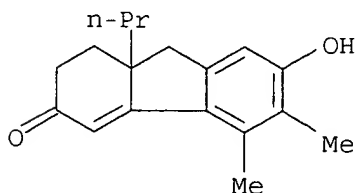
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L16 ANSWER 4 OF 9 REGISTRY COPYRIGHT 2001 ACS
 RN 101469-43-6 REGISTRY
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 (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN 3H-Fluoren-3-one, 5,6-dichloro-1,2,9,9a-tetrahydro-7-hydroxy-9a-propyl-,
 (.-.-.)-
 FS 3D CONCORD
 MF C16 H16 Cl2 O2
 SR CA
 LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
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1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

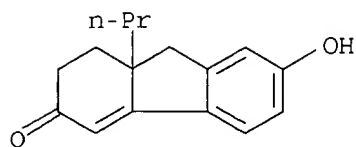
L16 ANSWER 5 OF 9 REGISTRY COPYRIGHT 2001 ACS
 RN 101375-45-5 REGISTRY
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 (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN 3H-Fluoren-3-one, 1,2,9,9a-tetrahydro-7-hydroxy-5,6-dimethyl-9a-propyl-,
 (.-.-.)-
 FS 3D CONCORD
 MF C18 H22 O2
 SR CA
 LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT
 (*File contains numerically searchable property data)



1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L16 ANSWER 6 OF 9 REGISTRY COPYRIGHT 2001 ACS
 RN 101375-44-4 REGISTRY
 CN 3H-Fluoren-3-one, 1,2,9,9a-tetrahydro-7-hydroxy-9a-propyl- (9CI) (CA
 INDEX NAME)
 OTHER CA INDEX NAMES:
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 FS 3D CONCORD
 MF C16 H18 O2
 SR CA
 LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT

(*File contains numerically searchable property data)



1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L16 ANSWER 7 OF 9 REGISTRY COPYRIGHT 2001 ACS

RN 101165-87-1 REGISTRY

CN 3H-Fluoren-3-one, 5,6-dichloro-1,2,9,9a-tetrahydro-7-hydroxy-9a-propyl-,
(9aR)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 3H-Fluoren-3-one, 5,6-dichloro-1,2,9,9a-tetrahydro-7-hydroxy-9a-propyl-,
(R) -

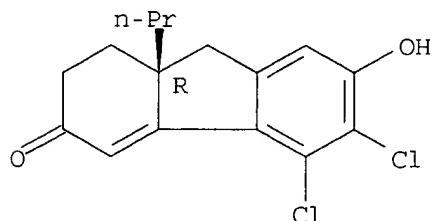
FS STEREOSEARCH

MF C16 H16 Cl2 O2

SR CA

LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



6 REFERENCES IN FILE CA (1967 TO DATE)

6 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L16 ANSWER 8 OF 9 REGISTRY COPYRIGHT 2001 ACS

RN 84226-62-0 REGISTRY

CN 3H-Fluoren-3-one, 5,6-dichloro-1,2,9,9a-tetrahydro-7-hydroxy-9a-methyl-,
(9CI) (CA INDEX NAME)

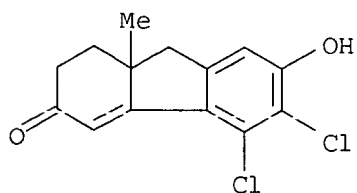
OTHER CA INDEX NAMES:

CN 3H-Fluoren-3-one, 5,6-dichloro-1,2,9,9a-tetrahydro-7-hydroxy-9a-methyl-,
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FS 3D CONCORD

MF C14 H12 Cl2 O2

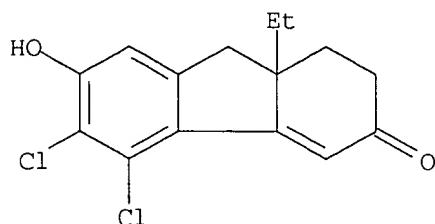
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, USPATFULL
(*File contains numerically searchable property data)



2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L16 ANSWER 9 OF 9 REGISTRY COPYRIGHT 2001 ACS
 RN 81997-15-1 REGISTRY
 CN 3H-Fluoren-3-one, 5,6-dichloro-9a-ethyl-1,2,9,9a-tetrahydro-7-hydroxy-
 (9CI) (CA INDEX NAME)
 OTHER CA INDEX NAMES:
 CN 3H-Fluoren-3-one, 5,6-dichloro-9a-ethyl-1,2,9,9a-tetrahydro-7-hydroxy-,
 (.-.-.)-
 DR 79796-62-6
 MF C15 H14 Cl2 O2
 LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, USPATFULL
 (*File contains numerically searchable property data)



7 REFERENCES IN FILE CA (1967 TO DATE)
 7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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FILE COVERS 1947 - 12 Aug 2001 VOL 135 ISS 8
 FILE LAST UPDATED: 10 Aug 2001 (20010810/ED)

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